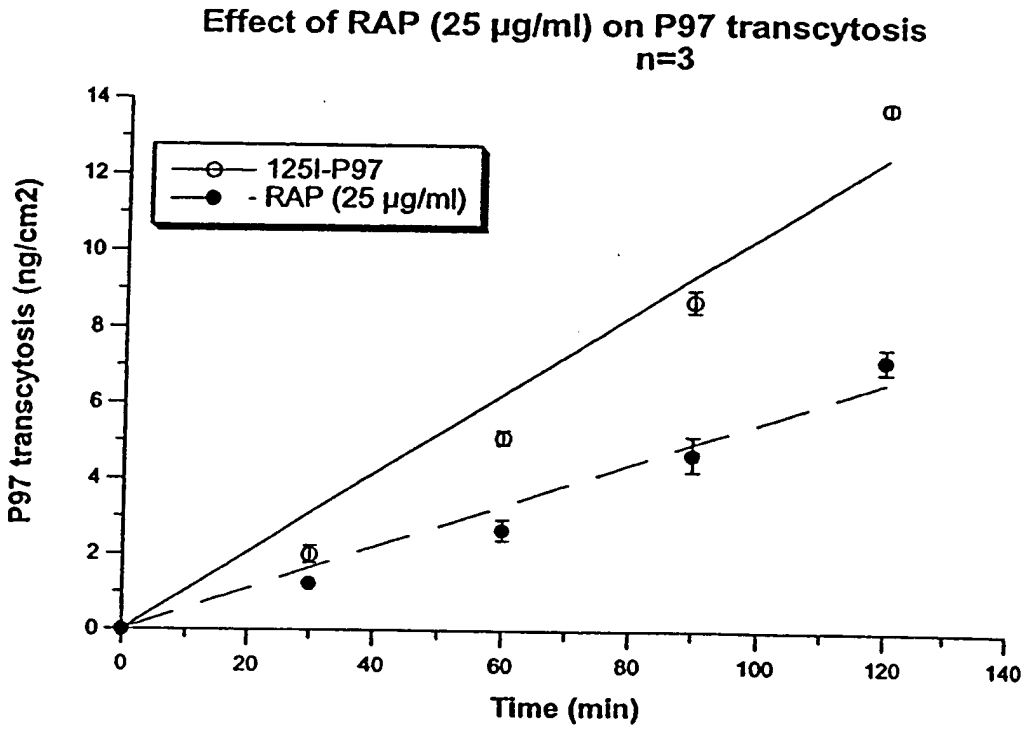
Effect of RAP (25 µg/ml) on P97 transcytosis
n=3
125I-P97
- RAP (25 µg/ml)
P97 transcytosis (ng/cm2)
Time (min)
0
2
4
6
8
10
12
14
0
20
40
60
80
100
120
140

FIGURE 1

**FIGURE 2a. Primers used to obtain sequences high-fidelity PCR amplification of human cDNA.**

RAPF: GCGATAGGATCCTACTCGCGGGAGAAGAACCAGCCCAAGCCGTCCCCGA

RAPR: GCGATAAACCGGTTTCTGCCTCGGCGCGAGCTCTGGAGATCCTGCCGGACAGGTCCT

GAAF: GCGATAACCGGTGCACACCCCGGCCGTCCCAGAGCAGTG

GAAR: GCGATACTCGAGTCAACACCAGCTGACGAGAAACTGC

IDUF: GCGATAACCGGTGAGGCCCCCCGCACCTGGTGCATGTGGACGCGGC

IDUR: GCGATACTCGAGTCATGGATTGCCCGGGGATGGGGGCCCTCTTGG

GDNF: ACAGTGACCGGTTCACCAGATAAACAAATGGCA

GDNR: ACAGTGCTCGAGTCTAGATCAGATACATCCACACCTTT

**FIGURE 2b. GDNF fusion, substitution of RAPF with RAPBACF in RAP amplification of GDNF construct.**

RAPBACF: ACAGTGGCCATGGGGGGTTCTTACTCGCGGGAGAAGAACCAGCCCAAGCCG

**FIGURE 3. Nucleotide and protein sequences of the RAP-GAA fusion**

```
cttaccgccatgcggggtccgagcggggctctgtggctgctcctggctctgcgcaccgtg
         M  R  G  P  S  G  A  L  W  L  L  L  A  L  R  T  V
ctcggatcctactcgcgggagaagaaccagcccaagccgtccccgaaacgcgagtccgga
 L  G  S  Y  S  R  E  K  N  Q  P  K  P  S  P  K  R  E  S  G
gaggagttccgcatggagaagttgaaccagctgtgggagaaggcccagcgactgcatctt
 E  E  F  R  M  E  K  L  N  Q  L  W  E  K  A  Q  R  L  H  L
cctcccgtgaggctggccgagctccacgctgatctgaagatacaggagagggacgaactc
 P  P  V  R  L  A  E  L  H  A  D  L  K  I  Q  E  R  D  E  L
gcctggaagaaactaaagcttgacggcttggacgaagatggggagaaggaagcgagactc
 A  W  K  K  L  K  L  D  G  L  D  E  D  G  E  K  E  A  R  L
atacgcaacctcaatgtcatcttggccaagtatggtctggacggaaagaaggacgctcgg
 I  R  N  L  N  V  I  L  A  K  Y  G  L  D  G  K  K  D  A  R
caggtgaccagcaactccctcagtggcacccaggaagacgggctggatgaccccaggctg
 Q  V  T  S  N  S  L  S  G  T  Q  E  D  G  L  D  D  P  R  L
gaaaagctgtggcacaaggcgaagacctctgggaaattctccggcgaagaactggacaag
 E  K  L  W  H  K  A  K  T  S  G  K  F  S  G  E  E  L  D  K
ctctggcgggagttcctgcatcacaaagagaaagttcacgagtacaacgtcctgctggag
 L  W  R  E  F  L  H  H  K  E  K  V  H  E  Y  N  V  L  L  E
accctgagcaggaccgaagaaatccacgagaacgtcattagcccctcggacctgagcgac
 T  L  S  R  T  E  E  I  H  E  N  V  I  S  P  S  D  L  S  D
atcaagggcagcgtcctgcacagcaggcacacggagctgaaggagaagctgcgcagcatc
 I  K  G  S  V  L  H  S  R  H  T  E  L  K  E  K  L  R  S  I
aaccagggcctggaccgcctgcgcagggtcagccaccagggctacagcactgaggctgag
 N  Q  G  L  D  R  L  R  R  V  S  H  Q  G  Y  S  T  E  A  E
ttcgaggagcccagggtgattgacctgtgggacctggcgcagtccgccaacctcacggac
 F  E  E  P  R  V  I  D  L  W  D  L  A  Q  S  A  N  L  T  D
aaggagctggaggcgttccgggaggagctcaagcacttcgaagccaaaatcgagaagcac
 K  E  L  E  A  F  R  E  E  L  K  H  F  E  A  K  I  E  K  H
aaccactaccagaagcagctggagattgcgcacgagaagctgaggcacgcagagagcgtg
 N  H  Y  Q  K  Q  L  E  I  A  H  E  K  L  R  H  A  E  S  V
ggcgacggcgagcgtgtgagccgcagccgcgagaagcacgccctgctggaggggcggacc
 G  D  G  E  R  V  S  R  S  R  E  K  H  A  L  L  E  G  R  T
aaggagctgggctacacggtgaagaagcatctgcaggacctgtccggcaggatctccaga
 K  E  L  G  Y  T  V  K  K  H  L  Q  D  L  S  G  R  I  S  R
gctcgcgccgaggcagaaaccggtgcacaccccggccgtcccagagcagtgcccacacag
 A  R  A  E  A  E  T  G  A  H  P  G  R  P  R  A  V  P  T  Q
tgcgacgtccccccaacagccgcttcgattgcgcccctgacaaggccatcacccaggaa
 C  D  V  P  P  N  S  R  F  D  C  A  P  D  K  A  I  T  Q  E
cagtgcgaggcccgcggctgctgctacatccctgcaaagcaggggctgcagggagcccag
 Q  C  E  A  R  G  C  C  Y  I  P  A  K  Q  G  L  Q  G  A  Q
atggggcagccctggtgcttcttcccacccagctaccccagctacaagctggagaacctg
 M  G  Q  P  W  C  F  F  P  P  S  Y  P  S  Y  K  L  E  N  L
agctcctctgaaatgggctacacggccaccctgacccgtaccacccccacctttcttcccc
 S  S  S  E  M  G  Y  T  A  T  L  T  R  T  T  P  T  F  F  P
aaggacatcctgaccctgcggctggacgtgatgatggagactgagaaccgcctccacttc
 K  D  I  L  T  L  R  L  D  V  M  M  E  T  E  N  R  L  H  F
acgatcaaagatccagctaacaggcgctacgaggtgcccttggagaccccgcgtgtccac
 T  I  K  D  P  A  N  R  R  Y  E  V  P  L  E  T  P  R  V  H
agccgggcaccgtccccactctacagcgtggagttctccgaggagcccttcggggtgatc
 S  R  A  P  S  P  L  Y  S  V  E  F  S  E  E  P  F  G  V  I
gtgcaccggcagctggacggccgcgtgctgctgaacacgacggtggcgcccctgttcttt
 V  H  R  Q  L  D  G  R  V  L  L  N  T  T  V  A  P  L  F  F
gcggaccagttccttcagctgtccacctcgctgccctcgcagtatatcacaggcctcgcc
 A  D  Q  F  L  Q  L  S  T  S  L  P  S  Q  Y  I  T  G  L  A
gagcacctcagtcccctgatgctcagcaccagctggaccaggatcaccctgtggaaccgg
 E  H  L  S  P  L  M  L  S  T  S  W  T  R  I  T  L  W  N  R
gaccttgcgcccacgcccggtgcgaacctctacgggtctcacccttttctacctggcgctg
 D  L  A  P  T  P  G  A  N  L  Y  G  S  H  P  F  Y  L  A  L
gaggacggcgggtcggcacacggggtgttcctgctaaacagcaatgccatggatgtggtc
```

```
  E  D  G  G  S  A  H  G  V  F  L  L  N  S  N  A  M  D  V  V
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  L  Q  P  S  P  A  L  S  W  R  S  T  G  G  I  L  D  V  Y  I
ttcctgggcccagagcccaagagcgtggtgcagcagtacctggacgttgtgggatacccg
  F  L  G  P  E  P  K  S  V  V  Q  Q  Y  L  D  V  V  G  Y  P
ttcatgccgccatactggggcctgggcttccacctgtgccgctggggctactcctccacc
  F  M  P  P  Y  W  G  L  G  F  H  L  C  R  W  G  Y  S  S  T
gctatcacccgccaggtggtggagaacatgaccagggcccacttccccctggacgtccaa
  A  I  T  R  Q  V  V  E  N  M  T  R  A  H  F  P  L  D  V  Q
tggaacgacctggactacatggactcccggagggacttcacgttcaacaaggatggcttc
  W  N  D  L  D  Y  M  D  S  R  R  D  F  T  F  N  K  D  G  F
cgggacttcccggccatggtgcaggagctgcaccagggcggccggcgctacatgatgatc
  R  D  F  P  A  M  V  Q  E  L  H  Q  G  G  R  R  Y  M  M  I
gtggatcctgccatcagcagctcgggccctgccgggagctacaggccctacgacgagggt
  V  D  P  A  I  S  S  S  G  P  A  G  S  Y  R  P  Y  D  E  G
ctgcggaggggggttttcatcaccaacgagaccggccagccgctgattgggaaggtatgg
  L  R  R  G  V  F  I  T  N  E  T  G  Q  P  L  I  G  K  V  W
cccgggtccactgccttccccgacttcaccaaccccacagccctggcctggtgggaggac
  P  G  S  T  A  F  P  D  F  T  N  P  T  A  L  A  W  W  E  D
atggtggctgagttccatgaccaggtgcccttcgacggcttgtggattgacatgaacgag
  M  V  A  E  F  H  D  Q  V  P  F  D  G  L  W  I  D  M  N  E
ccttccaacttcatcagaggctctgaggacggctgccccaacaatgagctggagaaccca
  P  S  N  F  I  R  G  S  E  D  G  C  P  N  N  E  L  E  N  P
ccctacgtgcctggggtggttgggggacccctccaggcggccaccatctgtgcctccagc
  P  Y  V  P  G  V  V  G  G  T  L  Q  A  A  T  I  C  A  S  S
caccagtttctctccacacactacaacctgcacaacctctacggcctgaccgaagccatc
  H  Q  F  L  S  T  H  Y  N  L  H  N  L  Y  G  L  T  E  A  I
gcctcccacagggcgctggtgaaggctcgggggacacgcccatttgtgatctcccgctcg
  A  S  H  R  A  L  V  K  A  R  G  T  R  P  F  V  I  S  R  S
acctttgctggccacggccgatacgccggccactggacgggggacgtgtggagctcctgg
  T  F  A  G  H  G  R  Y  A  G  H  W  T  G  D  V  W  S  S  W
gagcagctcgcctcctccgtgccagaaatcctgcagtttaacctgctgggggtgcctctg
  E  Q  L  A  S  S  V  P  E  I  L  Q  F  N  L  L  G  V  P  L
gtcggggccgacgtctgcggcttcctgggcaacacctcagaggagctgtgtgtgcgctgg
  V  G  A  D  V  C  G  F  L  G  N  T  S  E  E  L  C  V  R  W
acccagctgggggccttctacccccttcatgcggaaccacaacagcctgctcagtctgccc
  T  Q  L  G  A  F  Y  P  F  M  R  N  H  N  S  L  L  S  L  P
caggagccgtacagcttcagcgagccggcccagcaggccatgaggaaggccctcaccctg
  Q  E  P  Y  S  F  S  E  P  A  Q  Q  A  M  R  K  A  L  T  L
cgctacgcactcctcccccacctctacacactgttccaccaggcccacgtcgcgggggag
  R  Y  A  L  L  P  H  L  Y  T  L  F  H  Q  A  H  V  A  G  E
accgtggcccggcccctcttcctggagttccccaaggactctagcacctggactgtggac
  T  V  A  R  P  L  F  L  E  F  P  K  D  S  S  T  W  T  V  D
caccagctcctgtgggggggaggccctgctcatcaccccagtgctccaggccgggaaggcc
  H  Q  L  L  W  G  E  A  L  L  I  T  P  V  L  Q  A  G  K  A
gaagtgactggctacttcccccttgggcacatggtacgacctgcagacggtgccaatagag
  E  V  T  G  Y  F  P  L  G  T  W  Y  D  L  Q  T  V  P  I  E
gcccttggcagcctcccacccccacctgcagctccccgtgagccagccatccacagcgag
  A  L  G  S  L  P  P  P  P  A  A  P  R  E  P  A  I  H  S  E
gggcagtgggtgacgctgccggcccccctggacaccatcaacgtccacctccgggctggg
  G  Q  W  V  T  L  P  A  P  L  D  T  I  N  V  H  L  R  A  G
tacatcatccccctgcagggccctggcctcacaaccacagagtcccgccagcagcccatg
  Y  I  I  P  L  Q  G  P  G  L  T  T  T  E  S  R  Q  Q  P  M
gccctggctgtggccctaaccaagggtggagaggcccgaggggagctgttctgggacgat
  A  L  A  V  A  L  T  K  G  G  E  A  R  G  E  L  F  W  D  D
ggagagagcctggaagtgctggagcgaggggcctacacacaggtcatcttcctggccagg
  G  E  S  L  E  V  L  E  R  G  A  Y  T  Q  V  I  F  L  A  R
aataacacgatcgtgaatgagctggtacgtgtgaccagtgagggagctggcctgcagctg
  N  N  T  I  V  N  E  L  V  R  V  T  S  E  G  A  G  L  Q  L
cagaaggtgactgtcctgggcgtggccacggcgccccagcaggtcctctccaacggtgtc
  Q  K  V  T  V  L  G  V  A  T  A  P  Q  Q  V  L  S  N  G  V
```

```
cctgtctccaacttcacctacagccccgacaccaaggtcctggacatctgtgtctcgctg
 P  V  S  N  F  T  Y  S  P  D  T  K  V  L  D  I  C  V  S  L
ttgatgggagagcagtttctcgtcagctggtgttgactcgag
 L  M  G  E  Q  F  L  V  S  W  C  -
```

Melanotransferrin signal sequence is italicized. Linker peptide is underlined.

**FIGURE 4. Nucleotide and protein sequences of the RAP-IDU fusion**

```
aagcttaccgccatgcggggtccgagcggggctctgtggctgctcctggctctgcgcacc
          M  R  G  P  S  G  A  L  W  L  L  L  A  L  R  T
gtgctcggatcctactcgcgggagaagaaccagcccaagccgtccccgaaacgcgagtcc
 V  L  G  S  Y  S  R  E  K  N  Q  P  K  P  S  P  K  R  E  S
ggagaggagttccgcatggagaagttgaaccagctgtgggagaaggcccagcgactgcat
 G  E  E  F  R  M  E  K  L  N  Q  L  W  E  K  A  Q  R  L  H
cttcctcccgtgaggctggccgagctccacgctgatctgaagatacaggagagggacgaa
 L  P  P  V  R  L  A  E  L  H  A  D  L  K  I  Q  E  R  D  E
ctcgcctggaagaaactaaagcttgacggcttggacgaagatggggagaaggaagcgaga
 L  A  W  K  K  L  K  L  D  G  L  D  E  D  G  E  K  E  A  R
ctcatacgcaacctcaatgtcatcttggccaagtatggtctggacggaaagaaggacgct
 L  I  R  N  L  N  V  I  L  A  K  Y  G  L  D  G  K  K  D  A
cggcaggtgaccagcaactccctcagtggcacccaggaagacgggctggatgaccccagg
 R  Q  V  T  S  N  S  L  S  G  T  Q  E  D  G  L  D  D  P  R
ctggaaaagctgtggcacaaggcgaagacctctgggaaattctccggcgaagaactggac
 L  E  K  L  W  H  K  A  K  T  S  G  K  F  S  G  E  E  L  D
aagctctggcgggagttcctgcatcacaaagagaaagttcacgagtacaacgtcctgctg
 K  L  W  R  E  F  L  H  H  K  E  K  V  H  E  Y  N  V  L  L
gagaccctgagcaggaccgaagaaatccacgagaacgtcattagcccctcggacctgagc
 E  T  L  S  R  T  E  E  I  H  E  N  V  I  S  P  S  D  L  S
gacatcaagggcagcgtcctgcacagcaggcacacggagctgaaggagaagctgcgcagc
 D  I  K  G  S  V  L  H  S  R  H  T  E  L  K  E  K  L  R  S
atcaaccagggcctggaccgcctgcgcagggtcagccaccagggctacagcactgaggct
 I  N  Q  G  L  D  R  L  R  R  V  S  H  Q  G  Y  S  T  E  A
gagttcgaggagcccagggtgattgacctgtgggacctggcgcagtccgccaacctcacg
 E  F  E  E  P  R  V  I  D  L  W  D  L  A  Q  S  A  N  L  T
gacaaggagctggaggcgttccgggaggagctcaagcacttcgaagccaaaatcgagaag
 D  K  E  L  E  A  F  R  E  E  L  K  H  F  E  A  K  I  E  K
cacaaccactaccagaagcagctggagattgcgcacgagaagctgaggcacgcagagagc
 H  N  H  Y  Q  K  Q  L  E  I  A  H  E  K  L  R  H  A  E  S
gtgggcgacggcgagcgtgtgagccgcagccgcgagaagcacgccctgctggaggggcgg
 V  G  D  G  E  R  V  S  R  S  R  E  K  H  A  L  L  E  G  R
accaaggagctgggctacacggtgaagaagcatctgcaggacctgtccggcaggatctcc
 T  K  E  L  G  Y  T  V  K  K  H  L  Q  D  L  S  G  R  I  S
agagctcgcgccgaggcagaaaccggtgaggccccgcacctggtgcatgtggacgcggcc
 R  A  R  A  E  A  E  T  G  E  A  P  H  L  V  H  V  D  A  A
cgcgcgctgtggcccctgcggcgcttctggaggagcacaggcttctgccccccgctgcca
 R  A  L  W  P  L  R  R  F  W  R  S  T  G  F  C  P  P  L  P
cacagccaggctgaccagtacgtcctcagctgggaccagcagctcaacctcgcctatgtg
 H  S  Q  A  D  Q  Y  V  L  S  W  D  Q  Q  L  N  L  A  Y  V
ggcgccgtccctcaccgcggcatcaagcaggtccggacccactggctgctggagcttgtc
 G  A  V  P  H  R  G  I  K  Q  V  R  T  H  W  L  L  E  L  V
accaccaggggtccactggacggggcctgagctacaacttcacccacctggacgggtac
 T  T  R  G  S  T  G  R  G  L  S  Y  N  F  T  H  L  D  G  Y
ttggaccttctcagggagaaccagctcctcccagggtttgagctgatgggcagcgcctcg
 L  D  L  L  R  E  N  Q  L  L  P  G  F  E  L  M  G  S  A  S
ggccacttcactgactttgaggacaagcagcaggtgtttgagtggaaggacttggtctcc
 G  H  F  T  D  F  E  D  K  Q  Q  V  F  E  W  K  D  L  V  S
agcctggccaggagatacatcggtaggtacggactggcgcatgtttccaagtggaacttc
 S  L  A  R  R  Y  I  G  R  Y  G  L  A  H  V  S  K  W  N  F
gagacgtggaatgagccagaccaccacgactttgacaacgtctccatgaccatgcaaggc
 E  T  W  N  E  P  D  H  H  D  F  D  N  V  S  M  T  M  Q  G
ttcctgaactactacgatgcctgctcggagggtctgcgcgccgccagccccgccctgcgg
 F  L  N  Y  Y  D  A  C  S  E  G  L  R  A  A  S  P  A  L  R
ctgggaggccccggcgactccttccacaccccaccgcgatccccgctgagctggggcctc
 L  G  G  P  G  D  S  F  H  T  P  P  R  S  P  L  S  W  G  L
ctgcgccactgccacgacggtaccaacttcttcactggggaggcgggcgtgcggctggac
 L  R  H  C  H  D  G  T  N  F  F  T  G  E  A  G  V  R  L  D
```

```
tacatctccctccacaggaagggtgcgcgcagctccatctccatcctggagcaggagaag
 Y  I  S  L  H  R  K  G  A  R  S  S  I  S  I  L  E  Q  E  K
gtcgtcgcgcagcagatccggcagctcttccccaagttcgcggacacccccatttacaac
 V  V  A  Q  Q  I  R  Q  L  F  P  K  F  A  D  T  P  I  Y  N
gacgaggcggacccgctggtgggctggtccctgccacagccgtggagggcggacgtgacc
 D  E  A  D  P  L  V  G  W  S  L  P  Q  P  W  R  A  D  V  T
tacgcggccatggtggtgaaggtcatcgcgcagcatcagaacctgctactggccaacacc
 Y  A  A  M  V  V  K  V  I  A  Q  H  Q  N  L  L  L  A  N  T
acctccgccttcccctacgcgctcctgagcaacgacaatgccttcctgagctaccacccg
 T  S  A  F  P  Y  A  L  L  S  N  D  N  A  F  L  S  Y  H  P
cacccctcgcgcagcgcacgctcaccgcgcgcttccaggtcaacaacacccgcccgccg
 H  P  F  A  Q  R  T  L  T  A  R  F  Q  V  N  N  T  R  P  P
cacgtgcagctgttgcgcaagccggtgctcacggccatggggctgctggcgctgctggat
 H  V  Q  L  L  R  K  P  V  L  T  A  M  G  L  L  A  L  L  D
gaggagcagctctgggccgaagtgtcgcaggccgggaccgtcctggacagcaaccacacg
 E  E  Q  L  W  A  E  V  S  Q  A  G  T  V  L  D  S  N  H  T
gtgggcgtcctggccagcgcccaccgcccccagggcccggccgacgcctggcgcgccgcg
 V  G  V  L  A  S  A  H  R  P  Q  G  P  A  D  A  W  R  A  A
gtgctgatctacgcgagcgacgacacccgcgcccaccccaaccgcagcgtcgcggtgacc
 V  L  I  Y  A  S  D  D  T  R  A  H  P  N  R  S  V  A  V  T
ctgcggctgcgcggggtgccccccggcccgggcctggtctacgtcacgcgctacctggac
 L  R  L  R  G  V  P  P  G  P  G  L  V  Y  V  T  R  Y  L  D
aacgggctctgcagccccgacggcgagtggcggcgcctgggccggcccgtcttccccacg
 N  G  L  C  S  P  D  G  E  W  R  R  L  G  R  P  V  F  P  T
gcagagcagttccggcgcatgcgcgcggctgaggacccggtggccgcggcgccccgcccc
 A  E  Q  F  R  R  M  R  A  A  E  D  P  V  A  A  A  P  R  P
ttacccgccggcggccgcctgaccctgcgccccgcgctgcggctgccgtcgcttttgctg
 L  P  A  G  G  R  L  T  L  R  P  A  L  R  L  P  S  L  L  L
gtgcacgtgtgtgcgcgccccgagaagccgcccgggcaggtcacgcggctccgcgccctg
 V  H  V  C  A  R  P  E  K  P  P  G  Q  V  T  R  L  R  A  L
cccctgacccaagggcagctggttctggtctggtcggatgaacacgtgggctccaagtgc
 P  L  T  Q  G  Q  L  V  L  V  W  S  D  E  H  V  G  S  K  C
ctgtggacatacgagatccagttctctcaggacggtaaggcgtacaccccggtcagcagg
 L  W  T  Y  E  I  Q  F  S  Q  D  G  K  A  Y  T  P  V  S  R
aagccatcgaccttcaacctctttgtgttcagcccagacacaggtgctgtctctggctcc
 K  P  S  T  F  N  L  F  V  F  S  P  D  T  G  A  V  S  G  S
taccgagttcgagccctggactactgggcccgaccaggccccttctcggaccctgtgccg
 Y  R  V  R  A  L  D  Y  W  A  R  P  G  P  F  S  D  P  V  P
tacctggaggtccctgtgccaagagggcccccatccccgggcaatccatgactcgag
 Y  L  E  V  P  V  P  R  G  P  P  S  P  G  N  P  -
```

Melanotransferrin signal sequence is italicized. Linker peptide is underlined.

## FIGURE 5. Nucleotide and protein sequences of the RAP-GDNF fusion

```
atgggggttcttactcgcgggagaagaaccagcccaagccgtccccgaaacgcgagtcc
 M  G  G  S  Y  S  R  E  K  N  Q  P  K  P  S  P  K  R  E  S
ggagaggagttccgcatggagaagttgaaccagctgtgggagaaggcccagcgactgcat
 G  E  E  F  R  M  E  K  L  N  Q  L  W  E  K  A  Q  R  L  H
cttcctcccgtgaggctggccgagctccacgctgatctgaagatacaggagagggacgaa
 L  P  P  V  R  L  A  E  L  H  A  D  L  K  I  Q  E  R  D  E
ctcgcctggaagaaactaaagcttgacggcttggacgaagatggggagaaggaagcgaga
 L  A  W  K  K  L  K  L  D  G  L  D  E  D  G  E  K  E  A  R
ctcatacgcaacctcaatgtcatcttggccaagtatggtctggacggaaagaaggacgct
 L  I  R  N  L  N  V  I  L  A  K  Y  G  L  D  G  K  K  D  A
cggcaggtgaccagcaactccctcagtggcacccaggaagacgggctggatgaccccagg
 R  Q  V  T  S  N  S  L  S  G  T  Q  E  D  G  L  D  D  P  R
ctggaaaagctgtggcacaaggcgaagacctctgggaaattctccggcgaagaactggac
 L  E  K  L  W  H  K  A  K  T  S  G  K  F  S  G  E  E  L  D
aagctctggcgggagttcctgcatcacaaagagaaagttcacgagtacaacgtcctgctg
 K  L  W  R  E  F  L  H  H  K  E  K  V  H  E  Y  N  V  L  L
gagaccctgagcaggaccgaagaaatccacgagaacgtcattagcccctcggacctgagc
 E  T  L  S  R  T  E  E  I  H  E  N  V  I  S  P  S  D  L  S
gacatcaagggcagcgtcctgcacagcaggcacacggagctgaaggagaagctgcgcagc
 D  I  K  G  S  V  L  H  S  R  H  T  E  L  K  E  K  L  R  S
atcaaccagggcctggaccgcctgcgcagggtcagccaccagggctacagcactgaggct
 I  N  Q  G  L  D  R  L  R  R  V  S  H  Q  G  Y  S  T  E  A
gagttcgaggagcccagggtgattgacctgtgggacctggcgcagtccgccaacctcacg
 E  F  E  E  P  R  V  I  D  L  W  D  L  A  Q  S  A  N  L  T
gacaaggagctggaggcgttccgggaggagctcaagcacttcgaagccaaaatcgagaag
 D  K  E  L  E  A  F  R  E  E  L  K  H  F  E  A  K  I  E  K
cacaaccactaccagaagcagctggagattgcgcacgagaagctgaggcacgcagagagc
 H  N  H  Y  Q  K  Q  L  E  I  A  H  E  K  L  R  H  A  E  S
gtgggcgacggcgagcgtgtgagccgcagccgcgagaagcacgccctgctggaggggcgg
 V  G  D  G  E  R  V  S  R  S  R  E  K  H  A  L  L  E  G  R
accaaggagctgggctacacggtgaagaagcatctgcaggacctgtccggcaggatctcc
 T  K  E  L  G  Y  T  V  K  K  H  L  Q  D  L  S  G  R  I  S
agagctcgggccgaggcagaaaccggttcaccagataaacaaatggcagtgcttcctaga
 R  A  R  A  E  A  E  T  G  S  P  D  K  Q  M  A  V  L  P  R
agagagcggaatcggcaggctgcagctgccaacccagagaattccagaggaaaaggtcgg
 R  E  R  N  R  Q  A  A  A  A  N  P  E  N  S  R  G  K  G  R
agaggccagaggggcaaaaaccggggttgtgtcttaactgcaatacatttaaatgtcact
 R  G  Q  R  G  K  N  R  G  C  V  L  T  A  I  H  L  N  V  T
gacttgggtctgggctatgaaaccaaggaggaactgatttttaggtactgcagcggctct
 D  L  G  L  G  Y  E  T  K  E  E  L  I  F  R  Y  C  S  G  S
tgcgatgcagctgagacaacgtacgacaaaatattgaaaaacttatccagaaatagaagg
 C  D  A  A  E  T  T  Y  D  K  I  L  K  N  L  S  R  N  R  R
ctggtgagtgacaaagtagggcaggcatgttgcagacccatcgcctttgatgatgacctg
 L  V  S  D  K  V  G  Q  A  C  C  R  P  I  A  F  D  D  D  L
tcgtttttagatgataacctggtttaccatattctaagaaagcattccgctaaaaggtgt
 S  F  L  D  D  N  L  V  Y  H  I  L  R  K  H  S  A  K  R  C
ggatgtatctgatctaga
 G  C  I  -
```

Linker peptide is underlined.

Figure 6. Characterization of the RAP-GAA fusion.

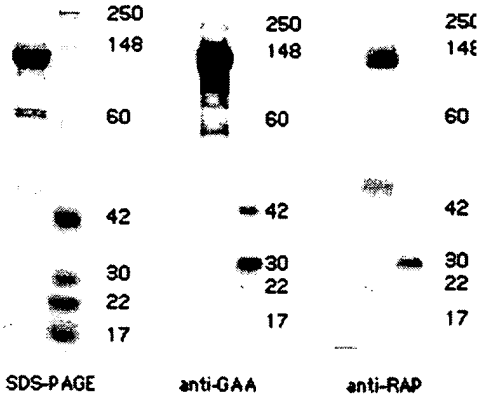


Figure 7. Assay for complex oligosaccharides on RAP-GAA

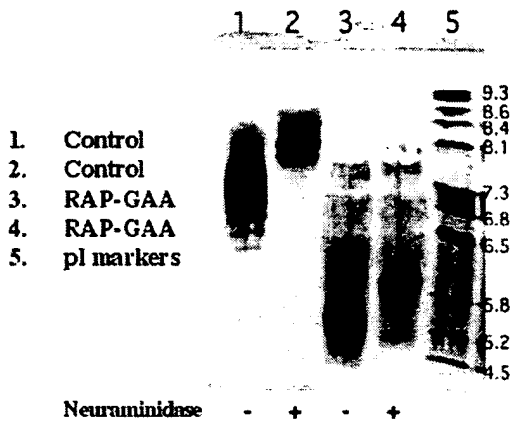


Figure 8. Assay for high-mannose oligosaccharides on RAP-GAA

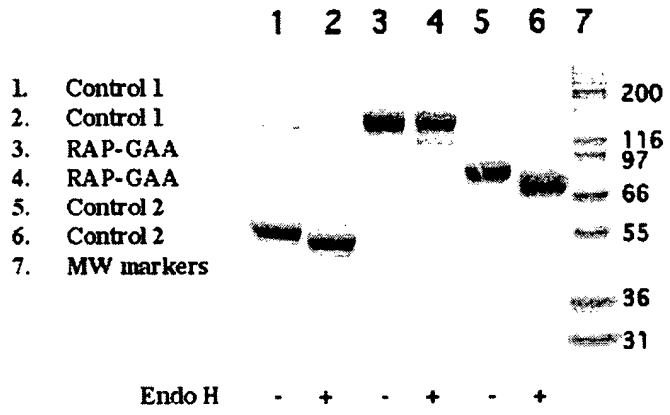
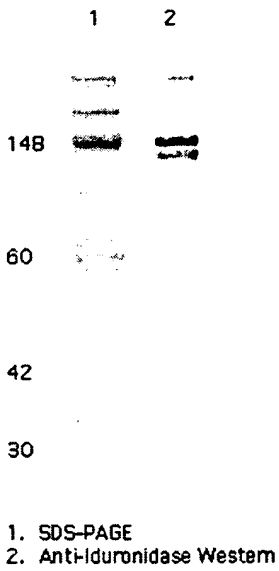


Figure 9. Characterization of RAP-IDU fusion




1. SDS-PAGE
2. Anti-Iduronidase Western

Binding of RAP and RAP-lysosomal enzyme fusion to LRP.

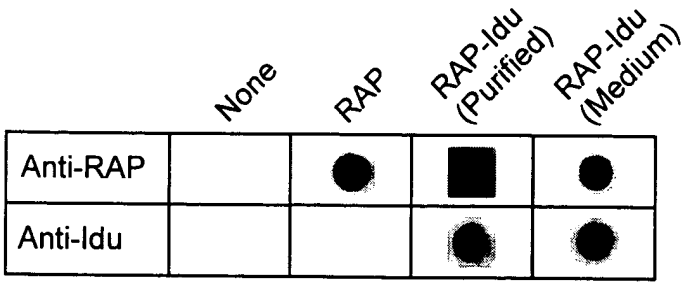
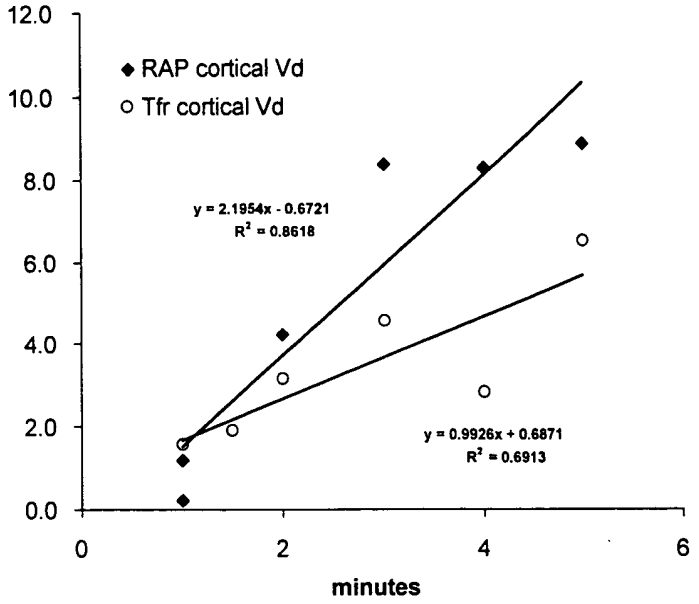
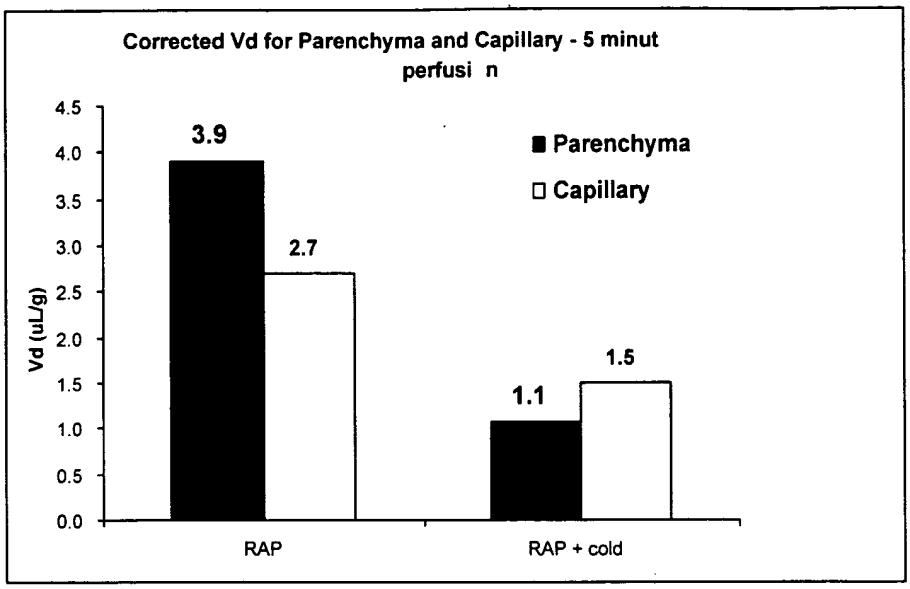



FIGURE 10



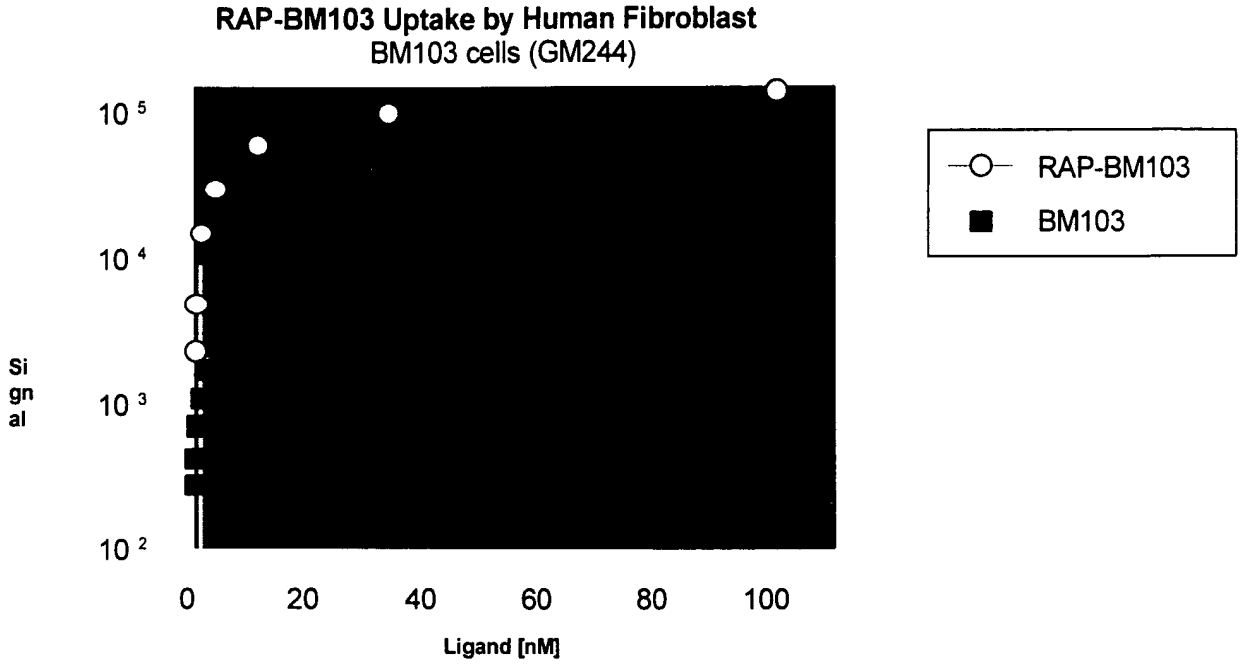

Corrected $V_d$ vs. Perfusion time.

FIGURE 11.




Distribution of RAP between brain capillary endothelium and brain parenchyma.

FIGURE 12.

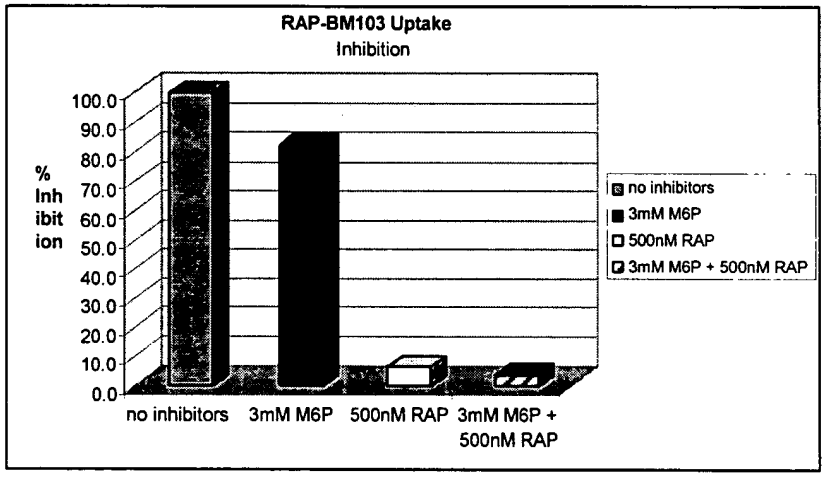



**RAP-BM103**

| Parameter | Value | Std. Error |
|---|---|---|
| Vmax | 160806 .4864 | 5540 .7619 |
| Km | 18 .6316 | 1 .8955 |

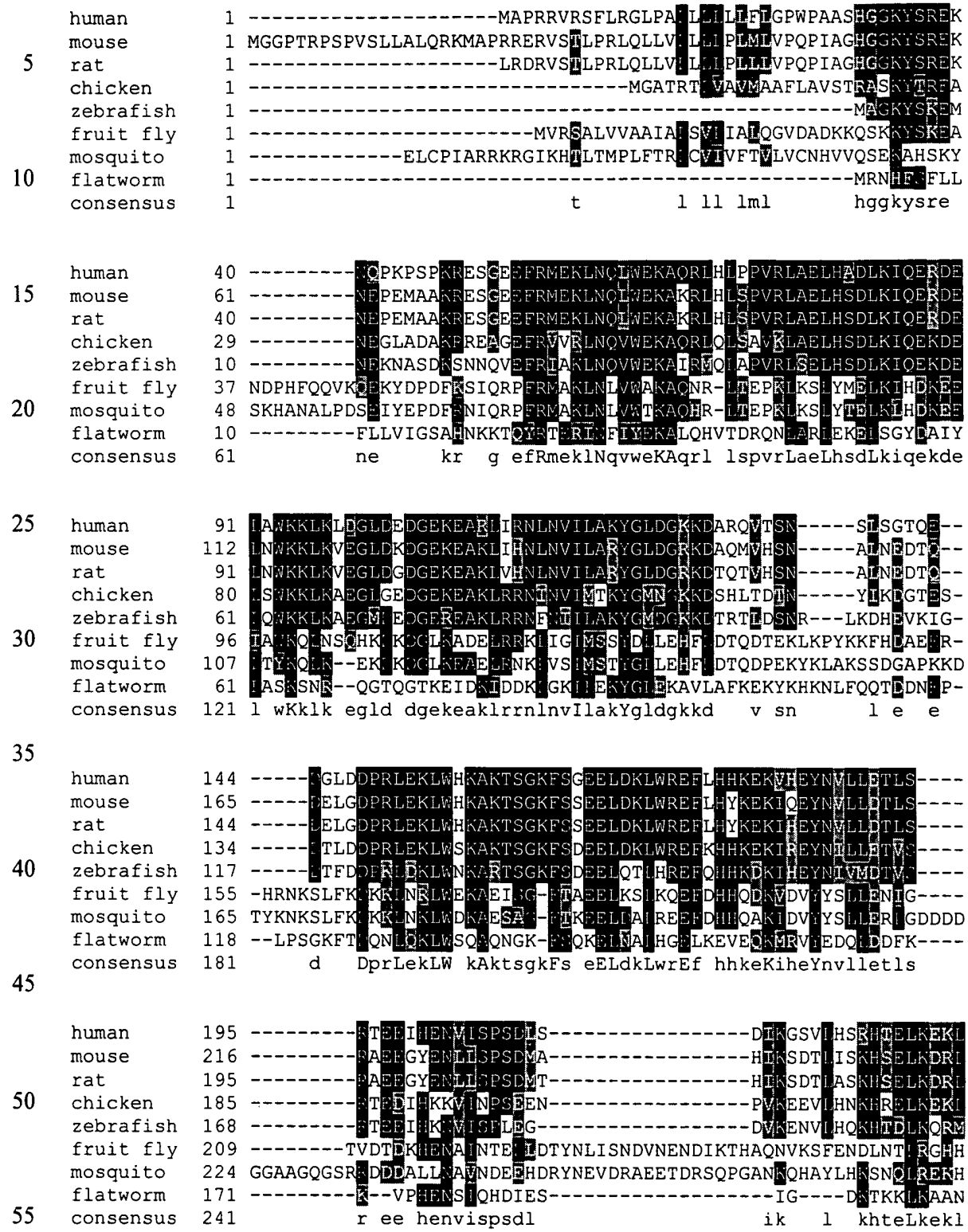
**BM103**

| Parameter | Value | Std. Error |
|---|---|---|
| Vmax | 2691 .6376 | 112 .1342 |
| Km | 1 .6615 | 0 .2002 |




# FIGURE 13

FIGURE 14. Multiple alignment of amino acid sequences of RAP from different species.



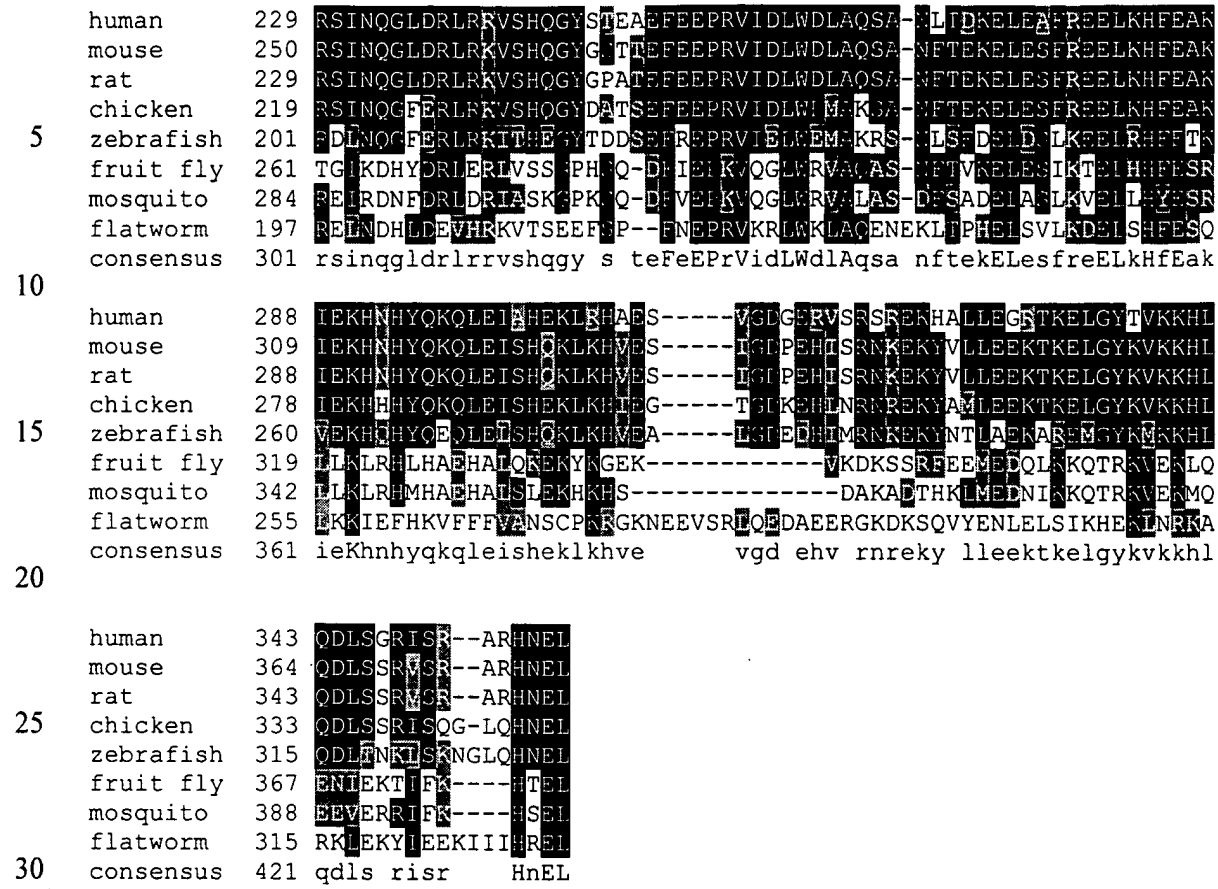

human 229
mouse 250
rat 229
chicken 219
zebrafish 201
fruit fly 261
mosquito 284
flatworm 197
consensus 301
human 288
mouse 309
rat 288
chicken 278
zebrafish 260
fruit fly 319
mosquito 342
flatworm 255
consensus 361
human 343
mouse 364
rat 343
chicken 333
zebrafish 315
fruit fly 367
mosquito 388
flatworm 315
consensus 421

**Figure 15: Amino Acid Sequence Of Human RAP (SEQ ID NO:1)**

TyrSerArgGluLysAsnGlnProLysProSerProLysArgGluSer
GlyGluGluPheArgMetGluLysLeuAsnGlnLeuTrpGluLysAla
GlnArgLeuHisLeuProProValArgLeuAlaGluLeuHisAlaAsp
LeuLysIleGlnGluArgAspGluLeuAlaTrpLysLysLeuLysLeu
AspGlyLeuAspGluAspGlyGluLysGluAlaArgLeuIleArgAsn
LeuAsnValIleLeuAlaLysTyrGlyLeuAspGlyLysLysAspAla
ArgGlnValThrSerAsnSerLeuSerGlyThrGlnGluAspGlyLeu
AspAspProArgLeuGluLysLeuTrpHisLysAlaLysThrSerGly
LysPheSerGlyGluGluLeuAspLysLeuTrpArgGluPheLeuHis
HisLysGluLysValHisGluTyrAsnValLeuLeuGluThrLeuSer
ArgThrGluGluIleHisGluAsnValIleSerProSerAspLeuSer
AspIleLysGlySerValLeuHisSerArgHisThrGluLeuLysGlu
LysLeuArgSerIleAsnGlnGlyLeuAspArgLeuArgArgValSer
HisGlnGlyTyrSerThrGluAlaGluPheGluGluProArgValIle
AspLeuTrpAspLeuAlaGlnSerAlaAsnLeuThrAspLysGluLeu
GluAlaPheArgGluGluLeuLysHisPheGluAlaLysIleGluLys
HisAsnHisTyrGlnLysGlnLeuGluIleAlaHisGluLysLeuArg
HisAlaGluSerValGlyAspGlyGluArgValSerArgSerArgGlu
LysHisAlaLeuLeuGluGlyArgThrLysGluLeuGlyTyrThrVal
LysLysHisLeuGlnAspLeuSerGlyArgIleSerArgAlaArgHis
AsnGluLeu

**Figure 16: Amino Acid Sequence of the 28 kD RAP polypeptide (SEQ ID NO:2)**

ProArgLeuGluLysLeuTrpHisLysAlaLysThrSerGlyLysPhe
SerGlyGluGluLeuAspLysLeuTrpArgGluPheLeuHisHisLys
GluLysValHisGluTyrAsnValLeuLeuGluThrLeuSerArgThr
GluGluIleHisGluAsnValIleSerProSerAspLeuSerAspIle
LysGlySerValLeuHisSerArgHisThrGluLeuLysGluLysLeu
ArgSerIleAsnGlnGlyLeuAspArgLeuArgArgValSerHisGln
GlyTyrSerThrGluAlaGluPheGluGluProArgValIleAspLeu
TrpAspLeuAlaGlnSerAlaAsnLeuThrAspLysGluLeuGluAla
PheArgGluGluLeuLysHisPheGluAlaLysIleGluLysHisAsn
HisTyrGlnLysGlnLeuGluIleAlaHisGluLysLeuArgHisAla
GluSerValGlyAspGlyGluArgValSerArgSerArgGluLysHis
AlaLeuLeuGluGlyArgThrLysGluLeuGlyTyrThrValLysLys
HisLeuGlnAspLeuSerGlyArgIleSerArgAlaArgHisAsnGlu
Leu